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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/823,373	03/30/2001	Sarita Chauhan	BC1032 US NA	7359

23906 7590 12/04/2003

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EXAMINER	
FREDMAN, JEFFREY NORMAN	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 12/04/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/823,373	CHAUHAN ET AL.	
	Examiner	Art Unit	
	Jeffrey Fredman	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 October 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,6-20,24-47 and 49* is/are pending in the application.

4a) Of the above claim(s) *3,4,6-8 and 24-45* is/are withdrawn from consideration.

5)☒ Claim(s) *10,12,14,20 and 47* is/are allowed.

6)☒ Claim(s) *1, 2, 9, 11, 13, 15-19, 46, 49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) ____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status

Claims 1-4, 6-20, 24-47 and 49 are pending.

Claims 5, 21-23, 48 are cancelled.

Claims 3, 4, 6-8 and 24-45 are withdrawn from consideration.

Claims 1, 2, 9, 11, 13, 15-19, 46, 49 are rejected.

Claims 10, 12, 14, 20 and 47 are allowed.

Any rejection which is not reiterated in this action is hereby withdrawn as no longer applicable.

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on July 17, 2003 has been entered.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 2 and 49 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to

reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In analysis of the claims for compliance with the written description requirement of 35 U.S.C. 112, first paragraph, the written description guidelines note regarding genus/species situations that "Satisfactory disclosure of a ``representative number'' depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed." (See: Federal Register: December 21, 1999 (Volume 64, Number 244), revised guidelines for written description.)

All of the current claims encompass a genus of nucleic acids which are different from those disclosed in the specification. The specification discloses several species of nitrilase enzyme sequences. However, the genus claimed includes variants for which no written description is provided in the specification. This is expressly permitted by the language of the specification and claim in which the percent homology language includes no functional requirement so that there is no common structure which must be preserved.

This large genus is represented in the specification by only the particularly named SEQ ID Nos. Thus, applicant has express possession of only two particular nitrilase sequences, in a genus which comprises hundreds of millions of different possibilities. Here, no common element or attributes of the sequences are disclosed, not even the presence of certain domains. No structural limitations or requirements

which provide guidance on the identification of sequences which meet these functional limitations is provided. Further, these claims encompass alternately spliced versions of the proteins, allelic variants including insertions and mutations, inactive precursor proteins which have a removable amino terminal end, and only specific nucleic and amino acid sequences have been provided. No written description of alleles, of upstream or downstream regions containing additional sequence, or of alternative splice variants has been provided in the specification.

It is noted in the recently decided case The Regents of the University of California v. Eli Lilly and Co. 43 USPQ2d 1398 (Fed. Cir. 1997) decision by the CAFC that

> "A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. See Fiers, 984 F.2d at 1169- 71, 25 USPQ2d at 1605- 06 (discussing Amgen). It is only a definition of a useful result rather than a definition of what achieves that result. Many such genes may achieve that result. The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See In re Wilder, 736 F.2d 1516, 1521, 222 USPQ 369, 372- 73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate."). Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material. "

In the current situation, the definition of the nitrilase gene using the hybridization language of paragraph (c) of claim 1 lack any specific required structure. Thus, these claims present precisely the situation of naming a type of material which is generally

known to likely exist, but, except for the two specific nitrilase sequences given fails to provide descriptive support for these generic claims.

It is noted that in Fiers v. Sugano (25 USPQ2d, 1601), the Fed. Cir. concluded that

> "...if inventor is unable to envision detailed chemical structure of DNA sequence coding for specific protein, as well as method of obtaining it, then conception is not achieved until reduction to practice has occurred, that is, until after gene has been isolated...conception of any chemical substance, requires definition of that substance other than by its functional utility."

As already noted, the current claims define the nitrilase nucleic acids solely by their functional utility, as fragments or components capable of hybridization to specific sequences, without any definition of the particular genus of sequences claimed.

In Vas-Cath Inc. v. Mahurkar (19 USPQ2d 1111, CAFC 1991), it was concluded that:

> "...applicant must also convey, with reasonable clarity to those skilled in art, that applicant, as of filing date sought, was in possession of invention, with invention being, for purposes of "written description" inquiry, whatever is presently claimed."

In the application at the time of filing, there is no record or description which would demonstrate conception of any nucleic acids other than those expressly disclosed which encode the nitrilase enzymes disclosed. Therefore, the claims fail to meet the written description requirement by encompassing sequences which are not described in the specification.

4. Claim 2 and 49 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

While the use of algorithms in a claim is not per se indefinite, the limitation to a 71% identity using the Needleman and Wunsch algorithm is indefinite where the specific parameters of the alignment are not given. For example, in that algorithm, parameters such as the gap value can vary. Thus, in the current case, where the prior art cited below has a 71.274% identity based upon a Smith-Waterman search using the parameters given on page 1, left side, and an 89% similarity, the claim is interpreted broadly to permit the prior art reference to anticipate the claim.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 1-2, 9, 11, 13 and 15 are rejected under 35 U.S.C. 102(b) as being anticipated by Kobayashi et al (Biochemistry (1992) 31:9000-9007).

Kobayashi et al teaches an isolated nucleic acid sequence fragment that encodes a nitrilase enzyme (see page 9004, figure 3) which sequence:

i) would hybridize to SEQ ID NO: 5 under the stated conditions,

ii) encompasses the completely complementary strand

iii) is 71.274 % identical to SEQ ID NO: 5 (see alignment).

With regard to the limitation in claim 5 that the nucleic acid be isolated from Acidovorax strain, in the absence of any structural limitations imposed by this claim limitation, this source designation is not given patentable weight. As MPEP 2111 notes

"During patent examination, the pending claims must be "given the broadest reasonable interpretation consistent with the specification". Here, the broadest reasonable interpretation is that the source gives no patentable weight. As MPEP 2113 notes "If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." Here, the only difference between the products is the claimed method of making. Since the products are the same given the scope of the claim, the products are anticipated.

Kobayashi further teaches expression of the nitrilase in an Escherichi coli host cell (see page 9001, column 1, subheading "Bacterial strains and Plasmids") which used the PUC18 vector that also comprises a Lac promoter consequently forming a chimeric gene which is operably linked to suitable regulatory sequences (see page 9001, column 1, subheading "Bacterial strains and Plasmids").

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation

under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 16-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kobayashi in view of Anderson et al (U.S. Patent 5,935,840).

Kobayashi teaches the limitations of claims 1-2, 9, 11, 13 and 15 as discussed above. Kobayashi does not teach the use of chromosomally integrated vectors or ribosome binding sites.

Anderson teaches the use of chromosomally integrated vectors and ribosome binding sites (see column 5, lines 23-38).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use the expression vector of Anderson to express the protein of Kobayashi since the use of a vector with a ribosome binding site will enhance the expression levels of the protein by more easily permitting the ribosomes to interact with the expressed mRNA and since integration of the vector will make the vector more stable and less likely to be lost from the cell, thereby enhancing efficient protein production.

10. Claim 46 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kobayashi in view of Anderson et al (U.S. Patent 5,935,840) and further in view of Galen (U.S. Patent 6,413,768).

Kobayashi in view of Anderson teach the limitations of claims 16-19 as discussed above. Kobayashi in view of Anderson do not teach the specific strains listed in claim 46.

Galen teaches MG1655 (See column 33, line 19).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use the cell of Galen to express the Nitrilase of Kobayashi since MPEP 2144.06 notes " Substituting equivalents known for the same purpose. In order to rely on equivalence as a rationale supporting an obviousness rejection, the equivalency must be recognized in the prior art, and cannot be based on applicant's disclosure or the mere fact that the components at issue are functional or mechanical equivalents. An express suggestion to substitute one equivalent component or process for another is not necessary to render such substitution obvious. In re Fout , 675 F.2d 297, 213 USPQ 532 (CCPA 1982)." Here, it is clear that Galen recognizes that MG1655 is a well known equivalent.

Allowable Subject Matter

11. Claims 10, 12, 14, 20 and 47 are allowed.

12. The following is a statement of reasons for the indication of allowable subject matter: These claims are drawn to specific deposited plasmids in microorganisms which deposits are not taught nor suggested by the prior art. Further, it is noted that the specification complies with the deposit rules on page 5, lines 25-34. With regard to claim 47, the sequence is novel and unobvious.

Response to Arguments

13. Applicant's arguments filed July 17, 2003 have been fully considered but they are not persuasive.

Applicant first argues the 112, first paragraph rejection. This rejection is only maintained against the claims which recite percent identity. When the facts of the current case are compared to those of Lilly, here there is 80% or 90% homology with nitrilase function. In Lilly, there was 81% homology with insulin function, a more defined activity. The Federal Circuit found that the specification lacked possession of the corresponding human sequence of the rat insulin gene even though they shared 81% homology. The issue in the USPTO written description guidelines is whether the structure plus the function is sufficient so that there is minimal variation among the species. In the current case, this expectation would not be met since the scope of the claim encompasses species with significant variation.

Applicant then argues the 112, second paragraph rejection. Applicant states that the default values used could be provided. This is not the issue. For a claim to be definite in this context, the default values must be in the claim. The fact that a certain program, as listed on page 26 of the specification, has certain default values, fails to inform which set of default values are limited by the claim. For example, the specification notes that the default value for gap extension penalty is 3. However, this value is not in the claim, which simply recites "default parameters". At http://www.hku.hk/bruhk/emboss/needle.html, the gap extension penalty default is 0.5. At http://www.gene-it.com/PDF/GenePASTexperimentV1.pdf, (attached) page 4, the

gap extension penalty is 2. So when the claim states "default parameters", what is the gap extension penalty, 0.5, 2 or 3? Currently, the algorithm is open to the use of any default values, and depending upon experimental choice, these values will give different results. Thus, an potential infringer might choose one set of default values and applicant another. A court would be unable to resolve which set of default values was actually the set required by the claim without the values being in the claim itself. Therefore, the claim remains indefinite. As a separate point, inclusion of the values requires basis in the specification, or else such an inclusion would be new matter and prohibited.

Applicant then argues the prior art rejection relying on Kobayashi. Applicant notes that the nitrilase enzyme of Kobayashi differs in its substrate specificity from the claimed enzyme. This argument is not, however, relevant to the claims. In order to anticipate the claims, Kobayashi must teach that the sequence does two things. Kobayashi must teach that the sequence encodes a nitrilase (see page 9004, figure 3). Second Kobayashi must teach a sequence which would hybridize under the conditions stated to SEQ ID NO: 5. The sequence of Kobayashi would hybridize to SEQ ID NO: 5 under the stated conditions based upon the percent identity. With regard to claim 2, Kobayashi meets the required percent identity. Consequently, Kobayashi anticipates the claim. With regard to claim 5, there is no structural limitation that is imposed by the choice of organism and consequently, no patentable limitation inherent in that choice.

With regard to Applicant's argument that the enzyme of Kobayashi does not have the same substrate specificity, thermal stability or reactivity as the enzyme encoded by

SEQ ID NO: 5, , it is noted that the features upon which applicant relies are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Since Kobayashi is maintained, the 103 rejections will also be maintained.

Applicant then argues this is an "obvious to try" situation. The legal standard for "reasonable expectation of success" is provided by caselaw and is summarized in MPEP 2144.08, which notes "obviousness does not require absolute predictability, only a reasonable expectation of success; i.e. , a reasonable expectation of obtaining similar properties. See , e.g. , In re O'Farrell , 853 F.2d 894, 903, 7 USPQ2d 1673, 1681 (Fed. Cir. 1988)." In this factual case, there is express suggestion in the prior art of Kobayashi that the nitrilase enzye could be expressed. There is further evidence as show in Anderson that vectors can be chromosomally integrated. This sufficient for a reasonable expectation of success. The MPEP cites In re O'Farrell, which notes regarding "obvious to try" at page 1682, that,

> "In some cases, what would have been "obvious to try" would have been to vary all parameters or try each of numerous possible choices until one possibly arrived at a successful result, where the prior art gave either no indication of which parameters were critical or no direction as to which of many possible choices is likely to be successful. E.g ., In re Geiger , 815 F.2d at 688, 2 USPQ2d at 1278; Novo Industri A/S v. Travenol Laboratories, Inc ., 677 F.2d 1202, 1208, 215 USPQ 412, 417 (7th Cir. 1982); In re Yates , 663 F.2d 1054, 1057, 211 USPQ 1149, 1151 (CCPA 1981); In re Antonie , 559 F.2d at 621, 195 USPQ at 8-9. In others, what was "obvious to try" was to explore a new technology or general approach

> that seemed to be a promising field of experimentation, where the prior art gave only general guidance as to the particular form of the claimed invention or how to achieve it. In re Dow Chemical Co ., 837 F.2d, 469, 473, 5 USPQ2d 1529, 1532 (Fed. Cir. 1985); Hybritech, Inc. v. Monoclonal Antibodies, Inc ., 802 F.2d 1367, 1380, 231 USPQ 81, 90-91 (Fed. Cir. 1 986), cert. denied , 107 S.Ct. 1606 (1987); In re Tomlinson ; 363 F.2d 928, 931, 150 USPQ 623, 626 (CCPA 1966).

The court in O'Farrell then, affirming the rejection, notes " Neither of these situations applies here." For the instant case, it is clear that neither situations applies here either. This is not a situation where the prior art suggests varying a variety of parameters, since the prior art directly points to the use of chromosomally integrated vectors by Anderson. This is also not a situation where only general guidance was given. The prior art provides specific guidance directing the use of the chromosomally integrated vectors.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Fredman whose telephone number is currently 703-308-6568. In mid January, 2004, when TC 1600 relocates to the new USPTO facility in Alexandria, the examiner's phone number will become 571-272-0742. The examiner can normally be reached on 6:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 703-308-1119. The supervisor's new telephone number in mid January will be 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is currently 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Jeffrey Fredman
Primary Examiner
Art Unit 1634